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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/775,909	02/02/2001	Mark Roberts	M0975/7006 (JRV)	9660

7590 01/25/2006

John R. Van Amsterdam
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, MA 02210

EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/775,909	ROBERTS, MARK	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37,39 and 41-55* is/are pending in the application.

4a) Of the above claim(s) *47-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37,39,41-46 and 55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10-31-05 has been entered.

Claims 1-36, 38 and 40 have been canceled. Claims 37, 39, 41-55 are pending. Claims 47-54 have been withdrawn from consideration.

Election/Restrictions

This application contains claims 47-54 drawn to an invention nonelected without traverse in the response filed 10-7-02. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Rejections Withdrawn

The objection to claim 43 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form is withdrawn in view of the amendments to the claims.

Rejections Maintained

Claims 37, 39, 41-44, 46 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Nencioni et al (Acta. Med. Rom. 29:78-83, 1991) or Podda et al (J. Exp. Med. 172:861-868, 1990) in view of Capiau et al (EP 352250, published 1-24-90), Tamura et al (U.S. Patent No. 5,182,109) and Honda et al (Japanese Application #3-

135923) made of record in the Office Action mailed 12-31-2002, for reasons made of record in the Office Action mailed 7-8-03 and herein.

Applicant's arguments have been carefully considered but are not persuasive. Applicant argues that the adjuvant property of the non-toxic double mutant (9 and 129) of pertussis toxin S1 subunit (also known as subunit A in the art) is unexpected. It is noted that the claim is not drawn to administering the double-mutant subunit alone. The claims presented and currently drafted provide for the administration of the double mutant form of pertussis toxin. Pertussis toxin is an A/B subunit toxin, therefore a fair reading of the claims encompasses the administration of the entire toxin wherein the A/B structure is maintained and the A subunit (S1 subunit) is present with the B subunit. There is nothing in the claims to provide for a purified A subunit to be administered in the absence of the B subunit. This interpretation of the claims is important in view of the record as to the relevance or lack thereof of the adjuvant activity of the B subunit of pertussis toxin. It is noted that the references as combined must be interpreted from the point of the skilled artisan, at the time that the invention was made. The time that the invention was made is the foreign priority date of late 1993, 10/5/93 To reach a proper determination under 35 U.S.C. 103, the examiner must step backward in time and into the shoes worn by the hypothetical "person of ordinary skill in the art" when the invention was unknown and just before it was made. In view of all factual information, the examiner must then make a determination whether the claimed invention "as a whole" would have been obvious at that time to that person. (MPEP 2142). It is well established that developments after the time of filing are of no consequence to what one skilled in the art would have believed at the time of filing (*In re Wright*, 27 USPQ2d 1510). Applicants have a two pronged argument 1) that it is unexpected that pertussis toxin comprising the S1 non-toxic double mutant (9 and 129) is unexpectedly an adjuvant and a mucosal adjuvant in particular and 2) that the art teaches away from the use of the claimed pertussis toxin comprising the S1 non-toxic double mutant because it was not believed at the time that the invention was

made that the S1 subunit was responsible for the adjuvant property. As to point 1, Applicants rely upon Roberts et al (1995), an article by Applicant, to teach that the mechanism(s) by which PTx exerts adjuvanticity is unknown but is thought to require an enzymatically active S1 subunit. This is not persuasive, this statement does not establish that this was the pervasive thought in the art at the time of filing. Applicants argue a reference relied upon in Roberts et al that is not of record. Applicants argue conclusions based on facts and evidence from a secondary reference that is not set forth in front of the examiner and therefore cannot be properly evaluated as to its teachings. Therefore, one cannot ascertain if these are later conclusions drawn by Roberts et al or the conclusions of the prior art. Further, as previously set forth, the art also believed that the B subunits had adjuvant activity (see Honda et al of record). As such, Roberts et al is not persuasive as providing a teaching away or unexpected results. Further, at the time that the invention was made it was believed in the art that the B subunits of the A/B bacterial toxins had adjuvant activity at the mucosal surface as evidenced by Tamura et al (US Patent 5,182,109 issued January 26, 1993). Applicants also apparently argue Holmgren et al teaches away from the combination because it teaches that the adjuvanticity of the toxins lie in the A subunit and mutation of the A subunit provides for loss of adjuvanticity. It is noted that the findings of Holmgren et al are in conflict with the findings of Tamura et al that provides evidence that the B subunit of CT and LT have adjuvant properties. Applicants argue that the findings of Honda et al, were later disproved by Tamura et al (1994). These later findings are not relevant to what one of ordinary skill in the art would have known at the time of filing. At the time of filing there is Honda et al and Tamura et al (US Patent 5,182,109) that establish that it was believed at the time that this invention was filed, that the B subunit had adjuvant activity. The later presented evidence disputing the earlier findings cannot be relied upon, because obviousness is established in view of the teachings of the art as a whole "at the time that the invention was made". This time period is not 1994 and not 1995, when the relied upon

articles were published. The claims are not drawn to use of the purified double mutant of the S1 subunit, in the absence of the S2 or B subunit. The claims merely require an "effective adjuvant amount of a non-toxic double mutant form of pertussis toxin", wherein the phase pertussis toxin has been interpreted to be the holotoxin (A+B). The claims do not require that the double mutant of A be administered alone or in the absence of the B subunit. Applicants also argue that whether or not a substance will act as an adjuvant is highly unpredictable. This is not persuasive, the adjuvant properties of the highly related bacterial toxins, cholera toxin, heat labile toxin from *E. coli* (LT) and pertussis toxin are demonstrated in the art at the time of filing. Pertussis toxin was a known mucosal adjuvant. As such, Applicant's arguments are not persuasive.

Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nencioni et al (Acta. Med. Rom. 29:78-83, 1991) or Podda et al (J. Exp. Med. 172:861-868, 1990); Capiau et al (EP 352250, published 1-24-90), Tamura et al (U.S. Patent No. 5,182,109) and Honda et al (Japanese Application #3-135923) as applied to claims 37-44 and 46 above and further in view of Halpern et al (Infection and Immunity 58(4):1004-1009, 1990) made of record in the Office Action mailed 12-31-2002, for reasons made of record in the Office Action mailed 7-8-03 and herein.

Applicant's arguments have been carefully considered but are not persuasive. Applicant argues that since the rejection for claim 37 falls for reasons made of record, so to should this rejection based on that same art. This is not persuasive, the art as combined for claim 37 does not fail for all the reasons made of record.

Citation of Relevant Art

Tamura et al (US Patent No. 5,182,109; issued January 26, 1993) teaches that cholera toxin (whole toxin), choler toxin B subunit, LT (whole toxin) and LTB (B subunit) are able to provide for adjuvant activity at the mucosal surface (se Examples 14-20).

Status of Claims

Claims 37, 39, 41-45, 46 and 55 stand rejected. Claims 47-54 are withdrawn from consideration as drawn to a noon-elected invention.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can normally be reached on M-Th 6:30 pm - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Smith Lynette can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patricia A. Duffy

Primary Examiner

Art Unit 1645